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Amendments to the Specification

Please replace the paragraph beginning on page 1, line 4, with the following rewritten paragraph:

— This application is a continuing application of U.S.S.N.s 60/113,968, filed December 28, 1998 and of 09/256,943, filed February 24, 1999, now U.S. Patent 6,429,027, issued August 6, 2002. —

Please replace the paragraph beginning on page 2, line 13, with the following rewritten paragraph:

— ~~U.S.S.N.s 08/818,199 and 09/151,877~~ U.S. Patent Nos. 6,023,540 and 6,327,410 describe array compositions that utilize microspheres or beads on a surface of a substrate, for example on a terminal end of a fiber optic bundle, with each individual fiber comprising a bead containing an optical signature. Since the beads go down randomly, a unique optical signature is needed to "decode" the array; i.e. after the array is made, a correlation of the location of an individual site on the array with the bead or bioactive agent at that particular site can be made. This means that the beads may be randomly distributed on the array, a fast and inexpensive process as compared to either the *in situ* synthesis or spotting techniques of the prior art. Once the array is loaded with the beads, the array can be decoded, or can be used, with full or partial decoding occurring after testing, as is more fully outlined below. —

Please replace the paragraph beginning on page 4, line 20, with the following rewritten paragraph:

— Generally, the array compositions of the invention can be configured in several ways. In a preferred embodiment, as is more fully outlined below, a "one component" system is used. That is, a first substrate comprising a plurality of assay locations (sometimes also referred to herein as "assay wells"), such as a microtiter plate, is configured such that each assay location contains an individual array. That is, the assay location and the array location are the same. For example, the plastic material of the microtiter plate can be formed to contain a plurality of "bead wells" in the bottom of each of the assay wells. Beads containing bioactive agents can then be loaded into the bead wells in each assay location as is more fully described below. It should be noted that while the disclosure herein emphasizes the use of beads, beads need not be used in any of the embodiments of the invention; the bioactive agents can be directly coupled to the array locations. For example, other types of arrays are well known and can be used in this format; spotted, printed or photolithographic arrays are well known; see for example

WO 95/25116; WO 95/35505; ~~PCT US98/09163~~ WO 98/50782; U.S. Patent Nos. 5,700,637; 5,807,522, ~~and~~ 5,445,934, ~~; and U.S.S.N.s 08/851,203 09/187,289~~ 6,023,540, and 6,327,410; and references cited within, all of which are expressly incorporated by reference. In one component systems, if beads are not used, preferred embodiments utilize non-silicon wafer substrates. —

Please replace the paragraph beginning on page 5, line 9, with the following rewritten paragraph:

— The present invention is generally based on previous work comprising a bead-based analytic chemistry system in which beads, also termed microspheres, carrying different chemical functionalities are distributed on a substrate comprising a patterned surface of discrete sites that can bind the individual microspheres. The beads are generally put onto the substrate randomly, and thus several different methodologies can be used to "decode" the arrays. In one embodiment, unique optical signatures are incorporated into the beads, generally fluorescent dyes, that could be used to identify the chemical functionality on any particular bead. This allows the synthesis of the candidate agents (i.e. compounds such as nucleic acids and antibodies) to be divorced from their placement on an array, i.e. the candidate agents may be synthesized on the beads, and then the beads are randomly distributed on a patterned surface. Since the beads are first coded with an optical signature, this means that the array can later be "decoded", i.e. after the array is made, a correlation of the location of an individual site on the array with the bead or candidate agent at that particular site can be made. This means that the beads may be randomly distributed on the array, a fast and inexpensive process as compared to either the in situ synthesis or spotting techniques of the prior art. These methods are generally outlined in ~~PCT US98/05025~~ WO 98/40726; ~~PCT US98/21193~~ WO 99/18434; ~~PCT US99/20914~~ WO 00/16101; ~~PCT US99/14387~~ WO 99/67641; and ~~U.S.S.N.s 08/818,199~~ 6,023,540; ~~09/315,584~~ 6,644,732; and ~~09/151,877~~ 6,327,410, all of which are expressly incorporated herein by reference. In addition, while the discussion herein is generally directed to the use of beads, the same configurations can be applied to cells and other particles; see for example ~~PCT US99/04473~~ WO 99/45357. —

Please replace the paragraph beginning on page 9, line 8, with the following amended paragraph:

— In a preferred embodiment, physical alterations are made in a surface of the substrate to produce the sites. In a preferred embodiment, for example when the second substrate is a fiber optic bundle, the surface of the substrate is a terminal end of the fiber bundle, as is generally

described in ~~08/818,199 and 09/151,877~~ 6,023,540 and 6,327,410, both of which are hereby expressly incorporated by reference. In this embodiment, wells are made in a terminal or distal end of a fiber optic bundle comprising individual fibers. In this embodiment, the cores of the individual fibers are etched, with respect to the cladding, such that small wells or depressions are formed at one end of the fibers. The required depth of the wells will depend on the size of the beads to be added to the wells. —

Please replace the paragraph beginning on page 20, line 12, with the following amended paragraph:

— In a preferred embodiment, the microspheres do not contain an optical signature. That is, as outlined in ~~U.S.S.N.s 08/818,199 and 09/151,877~~ U.S. Patent Nos. 6,023,540 and 6,327,410, previous work had each subpopulation of microspheres comprising a unique optical signature or optical tag that is used to identify the unique bioactive agent of that subpopulation of microspheres; that is, decoding utilizes optical properties of the beads such that a bead comprising the unique optical signature may be distinguished from beads at other locations with different optical signatures. Thus the previous work assigned each bioactive agent a unique optical signature such that any microspheres comprising that bioactive agent are identifiable on the basis of the signature. These optical signatures comprised dyes, usually chromophores or fluorophores, that were entrapped or attached to the beads themselves. Diversity of optical signatures utilized different fluorochromes, different ratios of mixtures of fluorochromes, and different concentrations (intensities) of fluorochromes. —